CLAIMS

1. A method for the manufacture of an oligonucleotide conjugate comprising the reaction of

(a) an oligonucleotide on a solid support having a labile orthogonal protecting group bound to a terminal hydroxy group, and

(b) a labeling compound,

wherein said labile orthogonal protecting group is at least partially substituted by said labeling compound in a nucleophilic substitution reaction.

2. The method according to claim 1, wherein the labeling compound is selected from the group consisting of peptides, enzymes, optically active compounds, antigenic epitopes, radioactive compounds, metal chelates, dyes, linker moieties, spacer moieties, charged residues, isotopically enriched mass labels, peptides, proteins, silicones, biotin, hydracids, lipids, steroids, multinuclear aromatic or, as applicable, heteroaromatic systems such as naphthalenes, anthracenes, xanthones, thioxanthones, acridones and the correspondingly substituted derivatives thereof as well as dinitrophenols, azobenzenes, psoralenes, fluoresceins, acridines, thiazoles, cyanines, coumarins and the correspondingly substituted derivatives thereof. Other preferred labeling compounds that can be used are monofunctional, bifunctional or polyfunctional long-chain or branched-chain alkanes, dendrimers, alkoxyalkyl compounds and, in particular, polyethylene glycols.

3. The method according to claim 2, wherein the labeling compound contains a reactive group selected from the group consisting of SH, OH, and NRH.

4. The method according to claim 3, wherein said NRH-group is part of a homocyclic, heterocyclic, homoaromatic, or heteroaromatic system, R being H, alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted alkylaryl.

5. The method according to one of claims 1 to 4, wherein said labile protecting group is selected from carbonate esters or thionocarbonate esters or N-alkylimidylcarbonate esters or dithiocarbonate esters or thiocarbamates of nitrophenyl, subst. nitrophenyl, pentahalogenphenyl, tetrahalogenphenyl, pyridyl, subst. pyridyl, N-alkyl-pyridinium-yl, imidazolyl, subst. imidazolyl, N-alkylimidazolyl, triazolyl, subst. triazolyl, tetrazolyl.

6. The method according to any one of claims 1 to 5, wherein the oligonucleotide and the resulting conjugate is bound to a solid phase at the 3′-end and the terminal hydroxyl group is the 5′-hydroxy group.

7. The method according to any one of claims 1 to 6, wherein the oligonucleotide and the resulting conjugate is bound to a solid phase at the 5′-end and the terminal hydroxyl group is the 3′-hydroxy group.

8. The method according to one of claims 1 to 7, characterized in that the oligonucleotide conjugate is only partially deprotected by said nucleophilic reaction.